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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/530,935	09/29/2000	Patrick Hearing	3927-4133US2	1381

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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/27/2002 11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/530,935	Applicant(s) HEARING ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) 20 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 29 September 2000 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *Notice to Comply* .

DETAILED ACTION

Non-Final Rejection

Claims 1-19 are pending examination.

Noncompliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Please reply to the sequence comply letter enclosed with this rejection.

Note: The response filed to this office action will be considered non-responsive, if the requirements of 37 CFR 1.821 through 1.825 are not met at the time the response is received.

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be to directed to Brian Whiteman, Art Unit 1635.

Specification

The disclosure is objected to because of the following informalities: the specification list sequences and a designated SEQ ID NO: for each sequence is not specified (See pages 5, 15, 27, 30-31, and 39. Appropriate correction is required.

Claim Objections

Claims 1-19 are objected to because of the following informalities: A claim can only contain one period and claims 1, 9, and 19 contain several periods. Claims 1-19 do not have the corresponding SEQ ID NO: for each sequence claimed. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 8, 18, and claims dependent therefrom are rejected under 35 U.S.C. 101 because the claims are not supported by either a well-asserted utility or a well-established utility.

Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS: repeated from http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" – Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, office personnel must determine if the assertion of utility is credible (i.e. whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based in inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific utility" – a utility that is *specific* to the subject matter claimed. This contrast with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what conditions can be diagnosed.

"Substantial utility" – a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying our further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic Research such as studying the properties of the claimed produce itself or the mechanisms in which the material is in involved.

B. A method of treating an unspecified disease or condition. (Note: this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor

substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. 101. This analysis should of course, be tempered by consideration of the context and nature of the invention. For example, if a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" – a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone, or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a non-specific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this were the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight, any carbon containing molecule would have a "well established utility" as a fuel since it can by burned; and any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

[See also the MPEP at 2107 –2107.02].

The claimed adenovirus vector (helper virus) in claims 8 and 18 are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. The reason for this is that the only utility for a helper virus is for use in making a replicant defective virion (See page 20 of the as-filed specification). The claimed adenovirus vector comprising an adenovirus packaging sequence having at least two copies of 5'-TTTGN8CG-3' and a plurality of COUP-TF binding sites comprising an A repeat VI element and a heterologous gene for expression in a host is not supported by a substantial utility because the disclosed use of the adenovirus vector is not for delivering a nucleic acid to a host. The specification states that, "It has been found that over-expression of COUP-TF in cells infected with adenovirus specifically represses virus production, in particular virus packaging (page 6)." More specifically, the specification states that, "Thus, adenovirus vectors of the present invention may contain one or more COUP-TF binding sites," and "an adenovirus containing a repressor binding site, propagating this vector in the absence of the repressor and repressing the packaging of said vector in the presence of the repressor (e.g. COUP-TF) (page 6)."

Furthermore, the specification states, "The vector design also increases the safety of recombinant adenovirus vectors for use in DNA transfer by reducing the potential of replicant competent adenovirus (page 13)." The claimed adenovirus vector in claims 8 and 18 do not have an identified substantial utility. In addition, in view of the claims, one skilled in the art would determine that a helper virus comprising of a heterologous gene would require further research to identify and reasonably confirm a "real world" context of use and therefore, a substantial utility is not defined. Note: since the claimed invention is not supported by a substantial utility because of the reasons set forth above, credibility utility has not been assessed. In conclusion, neither the specification as filed nor any art of record discloses or suggests any property or activity for the adenovirus vector in claims 8 and 18, such that is could be used in a method of expressing a heterologous gene in a mammal.

The applicants' traversal that the specification enables claims 1-19 (see paper no. 10, pages 5-7) is acknowledged and found persuasive. Rejection of claims 1-19 under 35 U.S.C. 112, first paragraph is withdrawn.

However, a new rejection on the grounds that claims 1-19 are not enabled under 112, 1st follows:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Note: that the number used in the scope of enablement corresponds to the number listed in claims 1, 9, and 19 set forth in the disclosure.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) A method of regulating adenovirus packaging of a replicant defective adenovirus vector comprising the steps of: A) obtaining an adenovirus vector containing an adenovirus packaging element comprising a repressor binding site, wherein the binding site is located between, within, or surrounding an adenovirus packaging sequence, B) obtaining an adenovirus comprising: a) 5' and 3' AAV ITRs, b) a different adenovirus packaging element other than the packaging element in the adenovirus vector of A), c) a promoter operatively linked to a heterologous gene; C) propagating the vector from step A) and the vector from step B) in the absence of said packaging repressor used to inhibit the packaging of the vector from step A) in a cell *in vitro*; and D) repressing the packaging of the vector from step A) by adding a repressor to the cell of step C) or a second cell comprising the vectors propagated from step C); 9) A method of administering a replicant defective adenovirus vector to a mammal comprising the steps of: A) encapsidating an adenovirus vector comprising a) 5' and 3' AAV ITRs, b) a different adenovirus packaging element other than in the vector of claim 6 or 7, c) a promoter operatively linked to a heterologous gene, using the adenovirus vector from claim 6 or 7; B) isolating a replicant defective adenovirus vector from step A; and C) administering the vector from step B) to said mammal; 19) A method of administering a replicant defective adenovirus vector to a mammal comprising the steps of: A) encapsidating an adenovirus vector, comprising a) 5' and 3' AAV ITRs, b) a different adenovirus packaging element other than the packaging element used in the adenovirus vector of claim 10, c) a promoter operatively linked to a heterologous gene, using the

adenovirus vector from claim 10; B) isolating a replicant defective adenovirus vector from step A); and C) preparing the replicant defective adenovirus vector from step B) in a pharmaceutically acceptable carrier; and D) administering said vector from step C) to a mammal, and does not reasonably provide enablement for other claimed embodiments embraced by the breadth of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 8, 18 and claims dependent therefrom are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a well asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In view of the as-filed specification, one skilled in the art would determine that the claimed invention encompasses the production of an adenovirus vector (helper virus), which is used in a method of producing a replicant defective adenovirus. The specification states that, "A major goal of DNA delivery systems is to create a viral vector that lacks all viral coding sequences and only contains DNA of interest for delivery purposes plus minimal viral DNA sequences required for growth and production of the virus. To grow such a virion, a helper virus is required (page 3)." Furthermore, the as-filed specification states, "It is a further object of this invention to provide a novel means to specifically repress the production of a helper virus while allowing the production of an adenovirus vector during the preparation of the virus (page 4)." The claimed invention contemplates a helper virus comprises an adenovirus-packaging element (repressor binding site) that can be located between, within, or surrounding an adenovirus

packaging sequence and can be repressed by the addition of a repressor. The adenovirus-packaging element (comprising a repressor binding site) in the adenovirus vectors also referred, as the helper virus is different than the adenovirus vector comprising a heterologous gene operatively to a promoter, in order to avoid packaging of the helper virus, which could result in the production of replicant competent adenovirus. The helper virus is inhibited from packaging when it is introduced into an *in vitro* cell, which endogenously or exogenously expresses a repressor (e.g. lac or COUP-TF). However, in view of the as-filed specification, the claims only encompass making and using the helper virus that is not intended to express a heterologous gene (see claim 8), but rather it is intended for use in making a replicant defective adenovirus comprising a heterologous gene used in a method for expression the heterologous gene in a mammal (see page 20).

An example of the claim not teaching one skilled in the art how to use the claimed invention is claim 9. Claim 9 reads on a method of administering an adenovirus to a mammal comprising the steps of: a) encapsidating the adenovirus vector of claim 8, thereby forming an adenovirus; b) isolating said adenovirus, c) preparing said adenovirus in a pharmaceutically acceptable carrier; and d) administering said adenovirus to the mammal (claim 8 is an adenovirus vector comprising: and adenovirus comprising an adenovirus packaging sequence containing a plurality of COUP-TF binding sites and an A repeat VI element and a heterologous gene for expression in a host). In view of the breadth of claim 9, it would take one skilled in the art an undue amount of experimentation to package an adenovirus with COUP-TF binding sites, an A repeat VI element, and a heterologous gene because the vector would not be package without the use of a helper virus or an adenovirus packaging cell line. In addition, the vector would not be

encapsidated because in view of what is taught by the specification (See Example 6), when the vector has the repressor binding sites, the vector would be unable to be encapsidated.

Thus, in view of the In re Wands Factors, the claimed invention is enabled for: 1) A method of regulating adenovirus packaging of a replicant defective adenovirus vector comprising the steps of: A) obtaining an adenovirus vector containing an adenovirus packaging element comprising a repressor binding site, wherein the binding site is located between, within, or surrounding an adenovirus packaging sequence, B) obtaining an adenovirus comprising: a) 5' and 3' AAV ITRs, b) a different adenovirus packaging element other than the packaging element in the adenovirus vector of A), c) a promoter operatively linked to a heterologous gene; C) propagating the vector from step A) and the vector from step B) in the absence of said packaging repressor used to inhibit the packaging of the vector from step A) in a cell *in vitro*; and D) repressing the packaging of the vector from step A) by adding a repressor to the cell of step C) or a second cell comprising the vectors propagated from step C); 9) A method of administering a replicant defective adenovirus vector to a mammal comprising the steps of: A) encapsidating an adenovirus vector comprising a) 5' and 3' AAV ITRs, b) a different adenovirus packaging element other than in the vector of claim 6 or 7, c) a promoter operatively linked to a heterologous gene, using the adenovirus vector from claim 6 or 7; B) isolating a replicant defective adenovirus vector from step A; and C) administering the vector from step B) to said mammal; 19) A method of administering a replicant defective adenovirus vector to a mammal comprising the steps of: A) encapsidating an adenovirus vector, comprising a) 5' and 3' AAV ITRs, b) a different adenovirus packaging element other than the packaging element used in the adenovirus vector of claim 10, c) a promoter operatively linked to a heterologous gene, using the

adenovirus vector from claim 10; B) isolating a replicant defective adenovirus vector from step A); and C) preparing the replicant defective adenovirus vector from step B) in a pharmaceutically acceptable carrier; and D) administering said vector from step C) to a mammal.

In conclusion, the as-filed specification and claims only provide sufficient guidance and/or evidence to reasonably enable the claimed invention listed above in the scope of enablement. One skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the application's disclosure, the unpredictability of making a helper virus comprising a heterologous gene for use in a method of expressing the heterologous gene in a mammal.

Applicants' traversal is not found persuasive because the applicants do not address the issues set forth above under 112 first.

Applicants traverse that the rejection under 112 second for claims 9 and 19 should be withdrawn because the applicants have amended that claims to address the Examiner's concerns. See page 4 of paper no. 10.

Applicants' traversal is acknowledged and is found persuasive because of the amendment to claims 9 and 19.

However, in view of the amended claims (claims 9-13 and 15-18) and originally filed (claims 8 and 14) a new ground of rejections follow:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 8-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The statement in claims 8-18, "**An** adenovirus vector according to claim" is indefinite because it does not point out which composition **an** adenovirus is referring to in the claim because the independent claims encompass one vector and the dependent claims refer to more than one vector. The dependent claims should state, "**The** adenovirus vector according to claim."

Applicants' traversal in paper no. 10 is not found persuasive in view of the new ground of rejection because it is not applicable to the new rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The applicants' traversal that the prior art does not teach an A repeat VI element in claims 6-15 (see paper no. 10, pages 7-8) is acknowledged and found persuasive. Rejections of claims 6-15 under 35 U.S.C. 102(b) are withdrawn.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635
3/22/02

DAVE T. NGUYEN
PRIMARY EXAMINER